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# Acute Tumor Lysis Syndrome in High Grade Lymphoblastic Lymphoma After a Prolonged Episode of Fever

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Acute tumor lysis syndrome occurs in rapidly growing lymphoid malignancies, usually as a consequence of chemotherapy or corticosteroids. We present what appears to be the first reported case of tumor lysis occurring after a sustained episode of high fever of 42.0° C in a patient with high grade lymphoblastic lymphoma and a high tumor burden. © 1996 Wiley-Liss, Inc.

**Key words:** tumor lysis, lymphoma, fever, hyperthermia, renal failure

## INTRODUCTION

*Acute tumor lysis* is the term that has been applied to a specific syndrome characterized by hypocalcemia, hyperphosphatemia, hyperuricemia, and acute renal failure [1]. It occurs most commonly in Burkitt's and non-Burkitt's lymphoma, high-grade non-Hodgkin's lymphoma, acute lymphoblastic leukemia, and chronic lymphocytic leukemia. A number of chemotherapeutic regimens have been associated with the development of this syndrome in these conditions [2]. Tumor lysis has also been reported after treatment with 2-chlorodeoxyadenosine [3], intrathecal methotrexate, and corticosteroids [5]. We present a case of a patient with malignant lymphoblastic lymphoma who developed acute tumor lysis after a prolonged febrile episode, with a maximum temperature of 42.0°C sustained for 2–3 hours.

## CASE REPORT

A 34-year-old white man was evaluated for progressive right arm weakness and pain for 3 weeks. He had been in remission after treatment for acute lymphocytic leukemia that was diagnosed in another institution and was treated with combination chemotherapy and whole brain irradiation. Physical examination showed inability to adduct the right arm above 10–15 degrees and patchy sensory loss in the right distal arm. There was no acute cervical, supraclavicular, axillary, or inguinal lymphadenopathy. The spleen was palpated 2 cm below the costal margin. The patient was hospitalized. Computer tomograpy (CT) of the chest, abdomen, and pelvis revealed extensive mediastinal and bilateal hilar adenopathy. There were streaky densities throughout the omentum and retroperitoneum. Computed tomography of the right neck revealed a 4 cm mass in the right brachial fossa. The patient was then scheduled for a CT guided-needle biopsy of this mass. He was taking no medications. Blood urea nitrogen was 17 mg/dl, potassium 4.6 mEq/L, lactate dehydrogenase (LDH) 1,014 U/L, calcium 10.4 mg/dl, and uric acid 9./8 mg/dl.

The patient became febrile the night before the biopsy. His maximum temperature was 42°C and persisted for 2–3 hours before being brought down to 38.8°C with acetaminophen 650 mg po. Potassium was 4.7 mEq/L, creatinine 0.9 mg/dl, blood urea nitrogen 42 mg/dl, pH 7.42, $PCO_2$ 45, $PO_2$ 95, and $HCO_3$ 29.2. On the second day the maximum temperature was 39.8°C. Potassium was 7.3 mEq/l, uric acid 18.6 mg/dl, lactate dehydrogenase 2,328 u/l, calcium 7.9 mg/dl, and creatinine 2.4 mg/dl. On the subsequent day creatinine rose to 4.7 mg/dl. pH was 7.43, $PCO_2$ 39, and $HCO_3$ 26. Blood cultures grew out group D streptococcus, and timentin 3.1 gm q6h was initiated. Acute renal failure supervened. The patient was transferred to the intensive care unit, where he slowly deteriorated, despite dialysis, and expired 1 week later.

Postmortem examination revealed massive orotracheal, mediastinal, hilar, para-aortic, mesenteric, and peripancreatic lymphadenopathy and splenomegaly, as well as tumor nodules on bilateral pleural surfaces, and a 5 cm mass deep in the right axilla. These all show in-

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volvement by a monotonous, small lymphocytic infiltrate. More then 90% of cells were reactive for L26 and 5% for UCHL-1. Histologically, necrosis was present in the center of the axillary mass. Sections from the lung, pleura, and pancreas showed this infiltrate as well. There was infiltration of left kidney medulla, pelvis, and cortex, as well as the right renal cortex.

Diagnosis of malignant lymphoma, lymphoblastic type (Working Formulation) was made based on postmortem tissue and bone marrow biopsy obtained 2 days antemortem. The bone marrow studies that established diagnosis of ALL in the past were reviewed and were felt, in retrospect, to reveal the same process. No immunophenotyping studies were performed at that time.

## DISCUSSION

Tumor lysis syndrome occurs predominantly in histologically aggressive lymphoid malignancies [2]. Characteristics that predict for the tumor lysis syndrome are thought to be high tumor burden, high lactic dehydrogenase (LDH), and renal insufficency [1,7]. The laboratory tumor lysis syndrome is defined by the occurrence of a 25% increase over baseline levels of phosphate, potassium, uric acid, and blood urea nitrogen or a 25% decline in serum calcium. Clinical tumor lysis syndrome occurs when there is also a rise in the serum creatinine level greater than 2.5 μg/dl, potassium level greater than 6 mEq/L or a decrease in calcium to less than 6 mEq/l, and development of life-threatening arrythmias or death [1]. It is reasonable to add the development of acute renal failure to this definition.

By these criteria, our patient clearly developed the tumor lysis syndrome. Unfortunately, phosphate levels were not obtained before or after the episode of fever. Other laboratory studies and the described clinical course, however, appear to be diagnostic. Although blood culture evidence of sepsis was obtained, the patient did not suffer hypotension or septic shock, and did not develop acidosis or disseminated intravascular coagulation. There was no evidence of hemolysis or rhabdomyolysis. The time frame to developing the renal failure is quite suggestive of tumor lysis as the precipitating cause.

The mechanisms by which hyperthermia induces acute cell kill are not completely understood. Areas of low blood perfusion in tumors may achieve higher temperatures than normal tissues and thus may be more susceptible to protein denaturation and cell death [8]. The extent of tissue damage appears to depend on the duration of exposure as well as absolute temperatures achieved [9]. Tumor lysis can occur spontaneously. A recent report presented the case of an 83-year-old female who developed a picture almost identical to that of our patient, but without fever [10].

Our case is, to the best of our knowledge, the first reported case of tumor lysis syndrome that occurred after a sustained episode of whole body hyperthermia secondary to fever. Inducing fever by injection of bacterial preparations was used to obtain a response in cancer patients by W. Coley, M.D., over a hundred years ago [11]. He, however, achieved higher body temperatures than that documented in our patient. The clinical circumstances of our case implicated hyperthermia as the cause of this patient's tumor lysis syndrome. The patient was on no medications, including corticosteroids, and his hyperuricemia, hyperkalemia, hypocalcemia, and renal failure were clearly temporally related to the febrile episode. Greater recognition of the possibility of developing this potentially fatal complication should lead to early initiation of hydration and antiuricemic therapy in febrile patients with high grade malignancies who have the risk factors for development of the tumor lysis syndrome.

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